

Office. A copy of the '885 is enclosed herewith. The applicants believe that the '885 claims in the U.S. application could interfere with the claims of the applicants' pending application.

Claim 5 of '885 claims

[a] vaccine composition which comprises an effective immunizing amount of an immunogenically active component of Claim 1, a pharmacologically acceptable carrier, and optionally an immunogenically stimulating adjuvant.

Claim 1 of '885 claims

[a]n immunogenically active component which comprises a member selected from the group consisting of merozoite antibody inducing, inactivated *Sarcocystis neurona* cells; tachyzoite antibody inducing, inactivated *Neospora hughesi* cells; a merozoite or tachyzoite antibody inducing antigen derived from said cells; DNA derived from said cells capable of inducing a merozoite or tachyzoite antibody immune response; and a mixture thereof. [emphasis added]

Claim 18 of '885 claims

A method for the prevention or amelioration of EPM disease in equines which comprises administering to said equine an immunogenically active component which comprises a member selected from the group consisting of merozoite antibody inducing, inactivated *Sarcocystis neurona* cells; tachyzoite antibody inducing, inactivated *Neospora hughesi* cells; a merozoite or tachyzoite antibody inducing antigen derived from said cells; DNA derived from said cells capable of inducing a merozoite or tachyzoite antibody immune response; and a mixture thereof. [emphasis added]

Applicants' Claim 4 claims a vaccine

"comprising . . . 16 ( $\pm$ 4) kDa *Sarcocystis neurona* antigen and a 30 ( $\pm$ 4) kDa *Sarcocystis neurona* antigen" which prevents disease caused by *Sarcocystis neurona* infection. The applicants' claimed vaccine is a species within the scope of the generic Claim 5 of '885. The 16 ( $\pm$ 4) kDa and 30 ( $\pm$ 4) kDa antigens are surface proteins which are found on the surface of merozoites or tachyzoites. Antisera from horses infected with *Sarcocystis neurona* contain antibodies against both antigens; therefore, the applicants' claimed vaccine containing the 16 ( $\pm$ 4) kDa and 30 ( $\pm$ 4) kDa antigens are antibody-inducing antigens within the scope of Claim 5 of the '885.

Applicants' Claims 13 and 45 claim a method for "inhibiting disease in an equid caused by a *Sarcocystis neurona* infection" using "a composition consisting essentially of a 16 ( $\pm$ 4) kDa antigen and a 30 ( $\pm$ 4) kDa antigen of *Sarcocystis neurona* . . . ." or "a composition that when injected into the equid causes the equid to produce antibodies against a 16 ( $\pm$ 4) kDa antigen and a 30 ( $\pm$ 4) kDa antigen . . . ." The applicants' claimed methods are species within the scope of the generic Claim 18 of '885 because the 16 ( $\pm$ 4) kDa and 30 ( $\pm$ 4) kDa antigens of the applicants' claims are species of the antibody-inducing antigens claimed in Claim 18 of the '885.

the applicants believe that Claims 4, 13, and 45 of the instant application and Claims 5 and 18 of the '885 application are drawn to the same patentable invention. 37 C.F.R. § 1.601(n) defines "same patentable invention" as when invention "A" is the same as an invention "B" when invention "A" is the same as (35 U.S.C. § 102) or is obvious (35 U.S.C. § 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

In light of 37 C.F.R. § 1.601(n), when the applicants' claimed vaccine consisting of the 16 ( $\pm$ 4) kDa and the 30 ( $\pm$ 4) kDa antigens of *Sarcocystis neurona* and method of use is considered to be prior art to the '885 application, then Claims 5 and 18 of the '885 application, which claim a vaccine comprising antibody-inducing antigens of *Sarcocystis neurona*, are anticipated by or made obvious by the applicants' invention. Therefore, the Claims 5 and 18 of the '885 application and Claims 4, 13, and 45 of the applicants' application are believed to claim the same patentable invention.

1. Claims 4-9, 13-17, 45-46, and 49-50 were rejected under 35 U.S.C. § 112, first paragraph.

In particular, the rejection stated that while the claims are drawn to vaccines comprising epitopes of

the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens, the sequences comprising the epitopes have not been identified or described.

Claims 4, 13, and 45 were amended in the applicants' response to the previous Office Action to claim a vaccine comprising both a 16 ( $\pm 4$ ) kDa antigen and a 30 ( $\pm 4$ ) kDa antigen (Claim 4), a method that uses a composition consisting essentially of both the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens (Claim 13), and a method that uses a composition which induces antibodies against both the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens (Claim 45). Thus, the claims are no longer limited to a mixture of particular epitopes of the antigens but to a mixture containing both antigens in their entirety.

The previously amended claims are believed to be enabled by the specification. The specification teaches isolating the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens from *Sarcocystis neurona* (paragraph bridging pages 33-34) and teaches a vaccine consisting of the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens (page 13, lines 1-5). Since the previously amended claims are directed to the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens *in toto* and not to particular epitopes in the antigens, knowledge of particular epitopes in the antigens is not necessary. Thus, one skilled in the art has no need for DNA or amino acid sequences. All one skilled in the art need do is

isolate the antigens from *Sarcocystis neurona* to make the applicants' claimed vaccine.

The applicants' claimed vaccine containing both the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens or method for using a composition containing both the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens to prevent disease caused by *Sarcocystis neurona* has not been described in the prior art.

In addition, applicants' claimed vaccine containing both the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens or method for using a composition containing both the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens to prevent disease caused by *Sarcocystis neurona* would not have been *prima facie* obvious over the prior art. Liang (1998) in particular, because while the prior art identifies a 16 kDa antigen and a 30 kDa antigen and states that the 16 kDa antigen might be useful in a vaccine (Liang (1998): page 1837, last para.), the prior art also states that the 30 kDa antigen induces non-inhibitory antibodies in horse serum (Liang (1998): page 1836, lines 4-5) which are not specific to *Sarcocystis neurona* (Liang (1998): page 1837, first para.). Therefore, in light of the prior art, a person of ordinary skill in the art would not have been motivated to make a vaccine or composition that contained both the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens to prevent disease caused by *Sarcocystis neurona*.

In light of the above, Claims 4-9, 13-17, 45-46, and 49-50 are enabled by the specification, thus satisfying 35 U.S.C. § 112, first paragraph. Reconsideration of the rejection is requested.

2. Claims 4-9, 13-17, 45-46, and 49-50 were rejected under 35 U.S.C. § 112, first paragraph.

In particular, the rejection stated that the specification does not provide a nexus between the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens and a functional vaccine comprising the same.

The applicants disagree. The prior art (Liang, (1998)) teaches that sera from horses with EPM contain antibodies against several antigens, including the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens. The prior art teaches that the 16 kDa antigen neutralizes *Sarcocystis neurona* infectivity (Liang (1998): Figure 2). The prior art teaches that there is an extensive body of data to indicate that antibodies to apicomplexan parasites is protective (Liang (1998): page 1836, discussion). The prior art teaches that most horses that are exposed to *Sarcocystis neurona* in the field develop effective immunity which may prevent the parasite from entering the central nervous system (Liang (1998): page 1834, third para.). The applicants teach that sera from horses with EPM contain antibodies which are specific to

the 30 ( $\pm 4$ ) kDa antigen of *Sarcocystis neurona*. Therefore, the 30 ( $\pm 4$ ) kDa antigen is involved in the immune response against *Sarcocystis neurona*. Thus, there is a nexus between a vaccine or composition containing the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens and a vaccine or composition which prevents disease caused by *Sarcocystis neurona* comprising the same.

Since horses with EPM have antibodies against the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens and many of these same horses develop immunity against the parasite, at a minimum it would be expected that a vaccine or composition comprising the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens would also induce antibodies against the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens and that some of the vaccinated horses will develop immunity against the parasite. The applicants' vaccine or composition does not have to provide good efficacy, it merely has to enable some horses to develop immunity to the parasite. Since many horses infected with *Sarcocystis neurona* do not have clinical symptoms and these same horses have antibodies against the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens, it is reasonable to expect that a vaccine containing the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens would provide protective immunity to at least some vaccinated horses. Therefore, the applicants' disclosure is sufficient to give a person of ordinary skill in the art a reasonable

expectation of success, particularly in light of PCT WO 01/80885 ('885) to Bigbie et al. which claims vaccines against *Sarcocystis neurona* comprising *Sarcocystis neurona* antigens and which shows that whole cell vaccines comprising *Sarcocystis neurona* are efficacious. In light of the applicants' disclosure, the '885, and the prior art, any unpredictability as to the efficacy of the applicants' composition would not be expected to be excessive.

While the applicants do not provide working examples of the vaccine or composition, working examples are not necessary to providing an enabling disclosure. Regardless of any working examples which could have been provided by the applicant, a person of ordinary skill in the art would most likely test a range of antigen concentrations anyway to determine which concentrations of antigens would be most efficacious in the artisan's hands. Because such experimentation would be considered prudent and routine by those of ordinary skill in the art, such experimentation would not be undue or overly burdensome.

With respect to the term "vaccine," the term encompasses (1) formulations that provide active immunological prophylaxis against a particular disease and (2) formulations that increase immunity to a particular disease. The Merriam Webster Collegiate

dictionary defines vaccine as "a preparation of killed microorganisms, living attenuated organisms, or living fully virulent organisms which is administered to produce or artificially increase immunity to a particular disease." The Merriam Webster Collegiate dictionary defines prophylactic as either (1) "guarding from or preventing disease" or (2) "tending to prevent or ward off [disease]." Thus, in its ordinary usage a vaccine can either "prevent" a particular disease or increase immunity to a particular disease which tends to ward off the disease. The applicants' claimed vaccine "inhibits" disease caused by *Sarcocystis neurona* which is embraced by the dictionary definition of "vaccine."

Liang (1988) teaches that the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens are surface antigens (See Liang (1988): Fig. 3). While it could be argued that antibodies induced by the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens may not kill the parasite, it is more than likely that because surface antigens are important to the biology of the parasite and the antibodies induced against the 16 ( $\pm 4$ ) and 30 ( $\pm 4$ ) kDa antigens bind to the antigens at the surface of the parasite, the induced antibodies would prevent or inhibit to some degree disease caused by the parasite. That supposition is clearly supported by the prior art (See Liang (1998): page 1837, second and third para.). Therefore, when the

applicants' specification is viewed in light of the state of knowledge in the art, the applicants' vaccine and composition containing the 16 ( $\pm$ 4) and 30 ( $\pm$ 4) kDa antigens for preventing disease caused by *Sarcocystis neurona* is adequately supported by the applicants' specification.

In light of the above, Claims 4-9, 13-17, 45-46, and 49-50 are adequately enabled by the specification, thus satisfying 35 U.S.C. § 112, first paragraph. Reconsideration of the rejection is requested. Notice of allowance is requested.

Respectfully,



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Encl. PCT WO 01/80885 A2 to Bigbie et al.